



CANADA'S MICHAEL SMITH  
G E N O M E  
**SCIENCES**  
C E N T R E

# exploring mutational evolution in metastatic colorectal cancer

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# introduction

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Colorectal cancer is the 2nd leading cause of cancer death in Canada<sup>1</sup>.

While survival from localized colorectal cancer is relatively good at 90%, only 12% of patients diagnosed with distant metastatic colorectal cancer will survive beyond 5 years<sup>2</sup>.

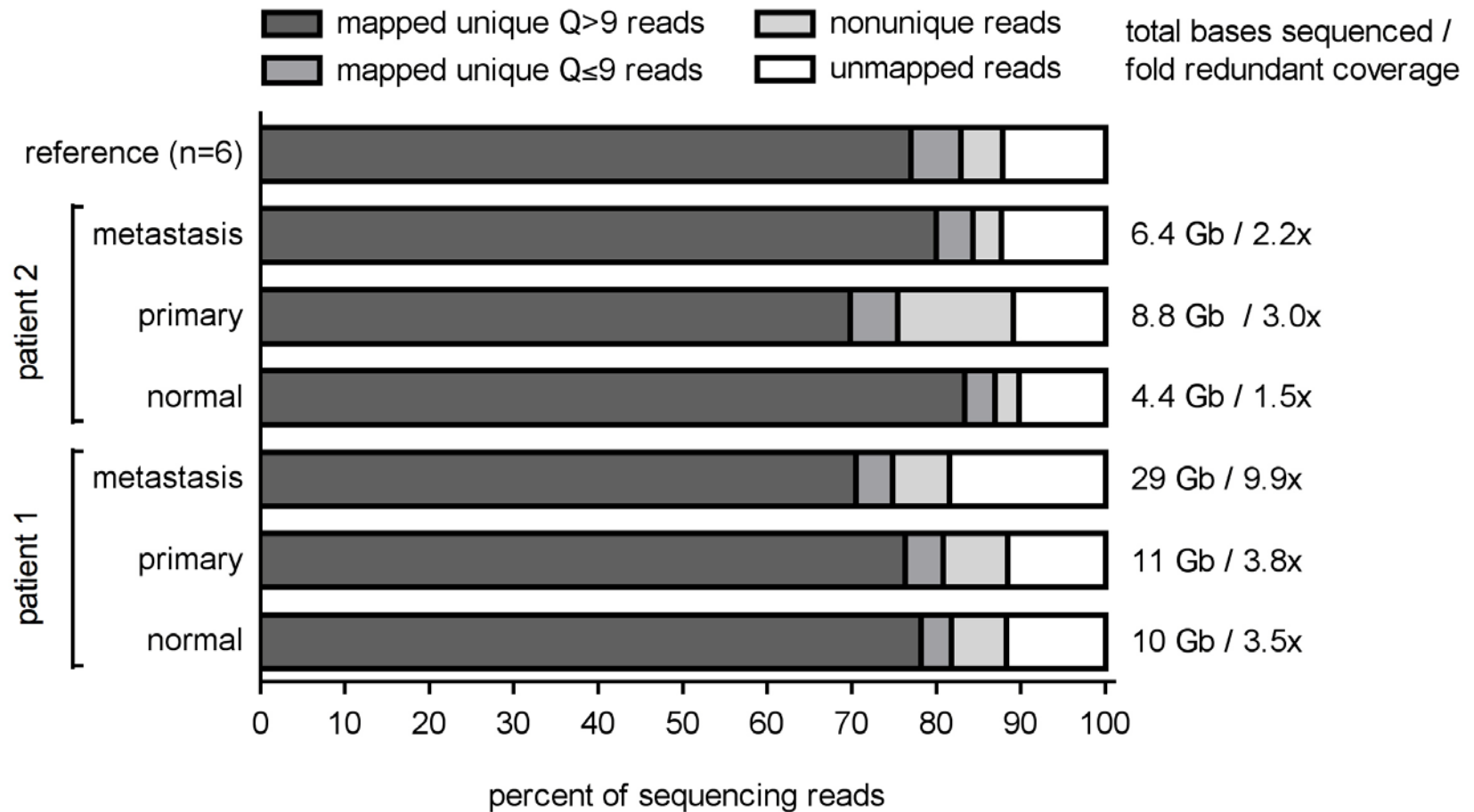
Considering the importance of metastasis to patients' prognoses, relatively little is known about the complement of acquired (i.e., somatic) mutations that specifically create, control, or direct metastases<sup>3</sup>.

## aims

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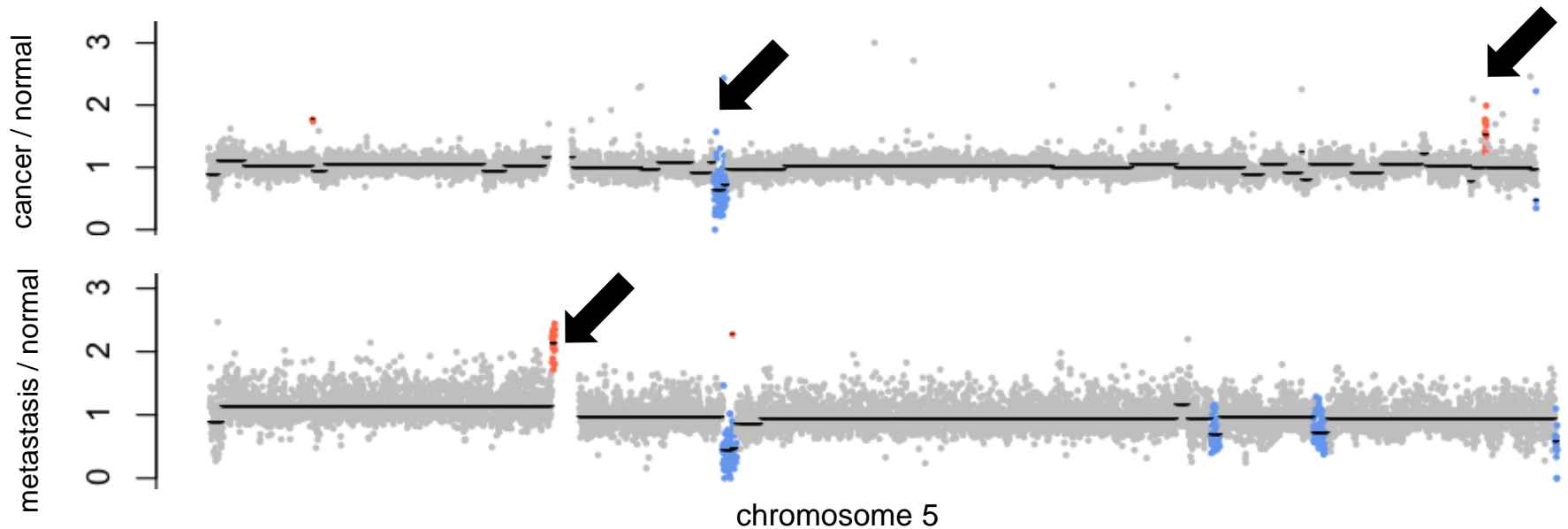
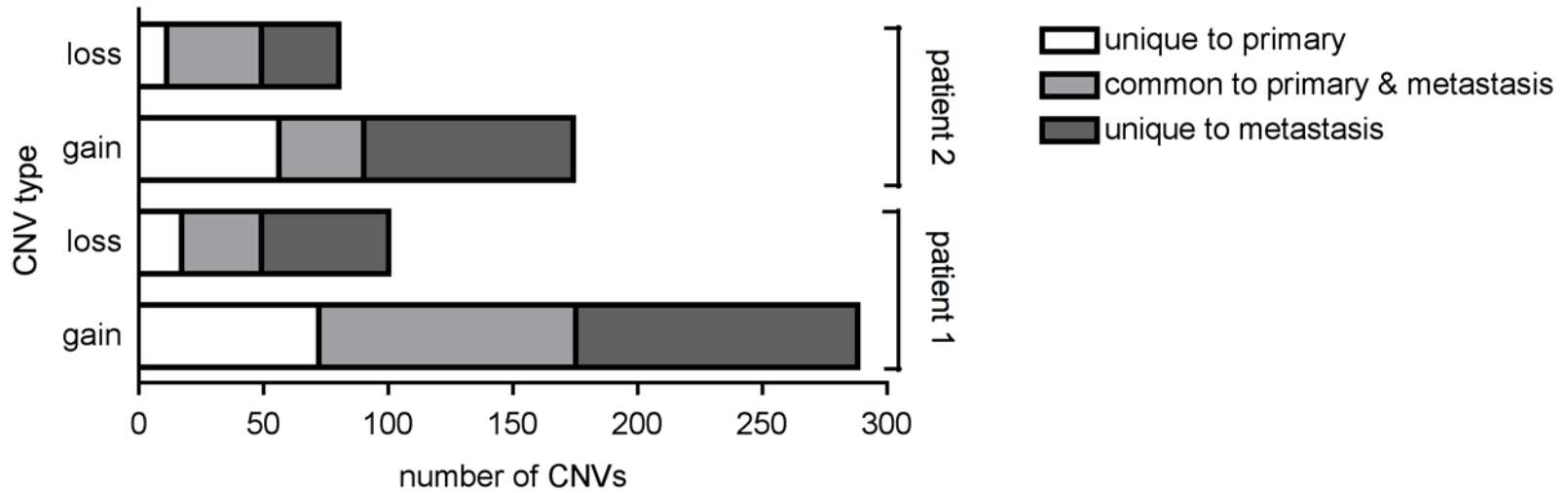
1. to discover genes that drive the spread and colonization of malignant cells from a primary colorectal tumor to the liver.
2. to show molecular evolution, at the level of CNVs, of normal tissue to primary colorectal cancer to liver metastasis.

# next-generation sequencing of DNA from FFPE tissue





# metastatic colorectal cancer evolves within patient

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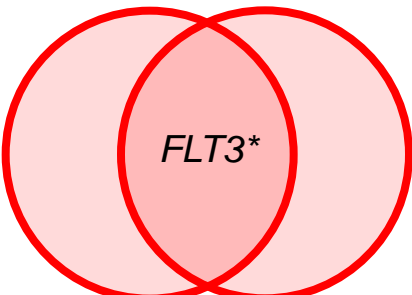
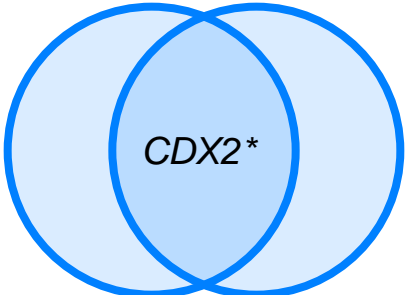


# deleted or amplified genes of interest between patient

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3500 |  unique to patient 1  
 common to patient 1 & 2

3000 |  unique to patient 1



\*Welcome Trust Sanger Institute COSMIC Catalogue Of Somatic Mutations In Cancer

# conclusions

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- It is possible to sequence formalin-fixed and paraffin-embedded samples using NGS technology (Schweiger, 2009).
- Primary colorectal cancers and their respective metastasis seem to be genetically similar but distinct.
- It may be possible to find genes of interest using this experimental paradigm.

# thank you

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The Marra Group

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Canadian Institutes of Health Research Fellowship

BC Cancer Foundation



Michael Smith Foundation for  
**Health Research**



**CIHR IRSC**  
Canadian Institutes of Health Research    Instituts de recherche  
en santé du Canada



**BC Cancer Agency**

CARE + RESEARCH

*An agency of the Provincial Health Services Authority*



**BC CANCER  
FOUNDATION**  
partners in discovery

# experimental plan

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## **identification of cases**

Dr. Sharlene Gill, gastrointestinal medical oncologist, British Columbia Cancer Agency, Vancouver

Identification of 42 cases from the BC Cancer Agency Vancouver

## **collection of cases**

Dr. David Owen, pathologist, Vancouver General Hospital

Requested and selected matched normal, primary tumor and liver metastasis archival tissue from British Columbia hospitals

## **molecular biology**

British Columbia Cancer Agency, Genome Sciences Centre

Nucleic acid extraction, library construction, next-generation sequencing

## **bioinformatics**

British Columbia Cancer Agency, Genome Sciences Centre

Alignment of reads to reference genome, QA/QC, FREEC

## **data analysis**

British Columbia Cancer Agency, Genome Sciences Centre

Identification of somatic mutations that have evolved and that are potential drivers of metastasis

